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	Mth	22-March-2000

Concerning: Comments on guidance for industry, photosafety testing, Docket No. 99D-5435, CDER 9967, Federal Register January 10, 2000 (Vol. 65, No. 6)

Dear ladies and gentlemen,

I appreciated very much your efforts to create a guidance for industry on photosafety testing. I reviewed the draft guidance, based on my long lasting earlier laboratory experience of in vitro and in vivo phototoxicity and photoallergenicity testing, and summarized some remarks on the next pages.

If you have questions to my comments or if I could be of any help on the finalization of the guidance paper, please let me know.

with the best personal regards,
sincerely yours

Thomas Maurer, Ph.D.

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Remarks on: Guidance for industry; photosafety testing. Docket No. 99D-5435, CDER 9967, Federal Register January 10, 2000 (Vol. 65, No. 6)

Page 2, Background
Two ways are described for the formation of the photoallergen. My experience is that the activation of the drug or chemical (=hapten) by light is necessary to bind with tissue proteins producing a complete allergen as stated for sulfanilamide. I think that the publications of Harber do not confirm that the formation of a photoproduct alone can lead to a complete allergen.

It is correct that fluoroquinolones have shown photocarcinogenic effects. I would recommend to add a reference to support that statement, such as Klecak G, Urbach F, Urwyler H, Fluoroquinolone antibacterials enhance UV-A induced skin tumors. J Photochem Photobiol B 1997; 37: 174-181.

Page 3, Background
To support the statement that chronic immunosuppressive therapy leads to higher cancer risk, it is recommended to add some newer publications; e.g. on relation of organ transplant patients and skin cancer.

Page 6, 2. Proposed approaches ...
I think that it is generally accepted that more than 90% of the photosensitivity reactions are dependent on the UV-A part of sunlight; a small part of reactions are UV-B dependent. The visible part plays no major role in light induced reactions.
Therefore, I would recommend to consider phototesting of drugs and chemicals that absorb light in the UV-B and UV-A range, but not generally in the visible part. The visible light range can be important for drugs used for the photodynamic therapy; I would recommend to limit testing with visible light for the specific purpose of photodynamic therapy.

Page 7, 2. Proposed approaches...
In the second last paragraph it is noticed that photosensitivity testing can be omitted when not sufficient levels of the photoactive drug are found in distribution studies in the skin or eye.
I doubht that this information is available for all drugs and that the quantitative aspects in tissue distribution of a photosensitizers are so clear to make a decision to perform or not perform studies.

Page 8, 4. Tests for evaluation of photosensitivity
I would recommend that two publications are added to this section.
1) The new edition of Dermatotoxicology Methods by Marzulli and Maibach (1998), Taylor&Francis, ISBN 1-56032-671-9.
2) A proposal prepared for the OECD on a standard protocol for phototoxicity testing (Nilsson R, Maurer T, Redmond N, A standard protocol for phototoxicity testing. Contact Dermatitis 1993; 28: 285-290).

Page 17, Glossary
Photoallergy: it should be mentioned that photoallergy can be induced after topical or systemic exposure to a drug or chemical.

Photoirritation / phototoxicity: It is correct that photoirritation and phototoxicity are nonimmunologic responses to a photoactive drug or chemical. Photoiritation is mainly used for photoreactions after topical exposure and phototoxicity for photoreactions after systemic exposure. It is recommended to add the different exposure situations in the glossary.

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